Clinical Investigation

Glycosylated Hemoglobin Measured by Affinity Chromatography in Diabetic and Nondiabetic Patients on Long-term Dialysis Therapy

ANTONIOS H. TZAMALOUKAS, MD; KATHY C. HSI, PhD; BARBARA J. QUINTANA, RN; TOBY L. MERLIN, MD; *and* PRATAP S. AVASTHI, MD, *Albuquerque*

We measured by affinity chromatography glycosylated hemoglobin levels in the blood of 43 diabetic and nondiabetic patients (139 measurements) on long-term dialysis therapy (continuous ambulatory peritoneal dialysis and hemodialysis) to determine the usefulness of this method of estimating glycemic control in diabetic persons on dialysis therapy. In nondiabetic patients, glycosylated hemoglobin levels were within the normal range (4.0% to 6.8% of total blood hemoglobin levels) for both continuous ambulatory peritoneal dialysis and hemodialysis. Glycosylated hemoglobin values correlated significantly with fasting blood glucose levels, serum urea levels, and serum total carbon dioxide content. By stepwise regression, fasting blood glucose values accounted statistically for .54 of the variability (R^2) in glycosylated hemoglobin. The contribution of the other variables to this variability was minimal. In 9 diabetic patients (3 on hemodialysis), glycosylated hemoglobin levels correlated significantly with average daily blood glucose levels. Regression of the fasting blood glucose value on glycosylated hemoglobin was similar between continuous ambulatory peritoneal dialysis and hemodialysis. Measuring glycosylated hemoglobin levels by affinity chromatography is a suitable method for assessing glycemia in dialysis patients.

(Tzamaloukas AH, Hsi KC, Quintana BJ, et al: Glycosylated hemoglobin measured by affinity chromatography in diabetic and nondiabetic patients on long-term dialysis therapy. West J Med 1989 Apr; 150:415-419)

We did this prospective study to determine whether glycosylated hemoglobin (hemoglobin [Hb] A_1) levels, measured by affinity chromatography, are appropriate for assessing glycemic control in diabetic patients on dialysis treatment. Nonenzymatic glycosylation of hemoglobin A posttranslation results in the four fractions, A_{1a1}, A_{1a2}, A_{1b}, and A_{1c}, that make up HbA_1.[1] The percent of HbA_1 in blood is proportional to the integrated blood glucose concentration.[1] Therefore, HbA_1 levels are measured to assess the control of glycemia in patients with diabetes mellitus.[1] In azotemic persons, HbA_1 measured by cation-exchange chromatography does not correlate with blood glucose levels because of interference of carbamylated hemoglobin with the assay of HbA_1.[2,3] Carbamylated hemoglobin is produced by a condensation of urea-derived isocyanic acid with the *N*-terminal amino groups of globin.[2] The use of HbA_1 levels as a measure of glycemia in patients with uremia has also been questioned for other reasons.[3,4] Nondiabetic patients with uremia have impaired glucose tolerance.[5] Uremia also shortens the life span of erythrocytes, and hemolysis decreases HbA_1 levels.[6] Finally, many uremic patients receive frequent transfusions of erythrocytes containing different concentrations of glycosylated hemoglobin.

Because a normal blood glucose level remains a desirable goal in diabetic persons on dialysis therapy,[7] a reliable indicator of integrated glycemia would be valuable in the care of these patients. Carbamylated hemoglobin does not interfere with the measurement of HbA_1 by affinity chromatography.[8] Certain questions regarding the appropriateness of affinity chromatography for HbA_1 determination in dialysis patients remain unanswered. This study addresses the following specific questions: Are HbA_1 levels normal in nondiabetic persons receiving dialysis? and Is glycemia the only blood measurement in dialysis patients statistically affecting HbA_1 levels? In clinical studies, significant correlations between HbA_1 levels and the degree of azotemia[8] and between HbA_1 levels and the degree of uremic acidosis[9] have been reported. Yet, glycosylation of hemoglobin is the same in azotemic and nonazotemic environments in vitro.[10]

Patients and Methods

The hemoglobin A_1 concentration was determined in fasting venous blood specimens of 43 patients on long-term dialysis therapy—two to four determinations per patient—over a period of six months. In the same blood specimens, a fasting blood glucose level, serum urea concentration, serum creatinine concentration, and serum total carbon dioxide (CO_2) content were also determined.

We studied four groups of patients: patients with diabetes on continuous ambulatory peritoneal dialysis (CAPD)

From the Departments of Medicine (Drs Tzamaloukas, Merlin, and Avasthi), Pathology (Dr Merlin), Community Medicine and Biostatistics (Dr Hsi), and the Dialysis Unit (Ms Quintana), Veterans Administration Medical Center and University of New Mexico School of Medicine, Albuquerque.

Reprint requests to Antonios H. Tzamaloukas, MD, Renal Section (111C), VA Medical Center, 2100 Ridgecrest Dr SE, Albuquerque, NM 87108.

ABBREVIATIONS USED IN TEXT

CAPD = continuous ambulatory peritoneal dialysis
Hb = hemoglobin

therapy (n = 9), diabetic persons on hemodialysis therapy (n = 8), nondiabetic persons on CAPD therapy (n = 11), and nondiabetic persons on hemodialysis therapy (n = 15). Of the 17 patients included in the diabetic groups, 16 had long-standing diabetes mellitus, either insulin-dependent or non-insulin-dependent; renal failure due to diabetic glomerulosclerosis, with typical clinical features; and one or more other end-organ manifestations of diabetes (retinopathy, 16 [100%]; neuropathy before renal failure, 16; gastroparesis, 12 [75%]; leg gangrene, 2 [13%]). In one patient with renal failure due to complications of nephrolithiasis, clinically overt diabetes developed several months after the initiation of hemodialysis, and this patient was included in the diabetic group on hemodialysis. This patient and one other diabetic person on hemodialysis therapy were not receiving insulin. All other diabetic patients on hemodialysis therapy and all diabetic patients on CAPD therapy were taking insulin during the study period.

The nondiabetic groups included patients with renal failure of diverse causes. The most common causes of renal failure were glomerulopathies and nephrosclerosis. Patients in the nondiabetic groups met two criteria: no past history of diabetes determined by reviewing clinical records and by patient interview, and fasting blood glucose levels that were consistently below 7.8 mmol per liter[7,11] after dialysis therapy was started. Postprandial blood glucose levels were not used as a criterion for ruling out diabetes, as they are difficult to interpret in uremic patients.[7] Three nondiabetic patients in the CAPD group and three in the hemodialysis group were classified as having impaired glucose tolerance by repeated fasting blood glucose levels between 6.4 and 7.8 mmol per liter.[7,11] Three of these patients had conditions known to be associated with impaired glucose tolerance, including advanced hepatic cirrhosis, pancreatic insufficiency, and a recent intake of corticosteroids.

A blood hemoglobin concentration was determined simultaneously with an HbA_1 measurement. The record of each patient in this study was reviewed for blood transfusions during the six months of the study and the four months before it. In contrast to patients on CAPD therapy, hemodialysis patients are not in a steady state of serum urea and creatinine concentrations and total CO_2 content. Therefore, for hemodialysis patients, postdialysis serum concentrations of these three variables were also determined. Time-averaged concentrations were then computed[12] and were included in the statistical analysis.

Hemoglobin A_1 levels were measured by boronate-affinity-gel column chromatography.[13(pp805-806)] The columns were manufactured by Endocrine Sciences, Tarzana, California. For the measurement, blood collected in ethylenediaminetetraacetic acid tubes was hemolyzed by adding deionized water, and a portion of the hemolysate was loaded on a column. The column was then washed with a buffer containing ammonium acetate, magnesium chloride, and sodium azide to remove the nonglycosylated hemoglobin and the rapid fractions of the glycosylated hemoglobin. A second buffer containing sorbitol was then applied to elute the HbA_1 from the column. The total hemoglobin level and the HbA_1 fraction were quantitated by absorbance at 414 nm in a Gilford spectrophotometer. Hemoglobin A_1 levels are reported as percentages of the total hemoglobin concentration in blood. Fasting blood glucose levels, serum urea and creatinine concentrations, and total CO_2 content were determined by a Beckman Astra-8 analyzer.

We computed the correlation between HbA_1 levels and the other named variables by pairs. Each measurement was taken to represent one data point (measurements = 139). When we did the same analysis using each patient's average as one data point (n = 43), the results were similar. The fasting blood glucose level may be a poor measure of integrated glycemia. Nine diabetic patients (six on CAPD therapy) had repeated blood glucose determinations (fasting and postprandial) during the days of drawing blood specimens for the HbA_1 assay. For these patients, we computed average daily glucose concentrations and compared them to HbA_1 levels. Between four and six blood specimens daily were needed for computing one average daily blood glucose level. The number of days averaged for one determination was between one and five with the days of the HbA_1 concentration in the middle if more than two days were averaged. Between one and four pairs of average daily blood glucose and HbA_1 values were available per patient (total 26).

Further statistical analysis was done on the interrelations of the five fasting variables. Initially the frequency distributions of these variables were examined by "stem-and-leaf" and "box" plots. By these methods, the frequency distributions were shown to be not normal, and one blood glucose level and four serum urea concentrations were identified as outliers. These findings indicate departures of the data distribution from statistical assumptions necessary for linear-regression models. The departures were corrected to a degree by logarithmic transformation of the variables and by omitting from the statistical analysis the observations identified as outliers. The logarithmically transformed variables were then entered in the stepwise-regression procedure[14] to search for the independent variables that have a high degree of regressive relation with HbA_1 levels.

Finally, we compared the regressions of blood glucose values on HbA_1 levels between patients receiving CAPD and hemodialysis patients. The rationale for this comparison was

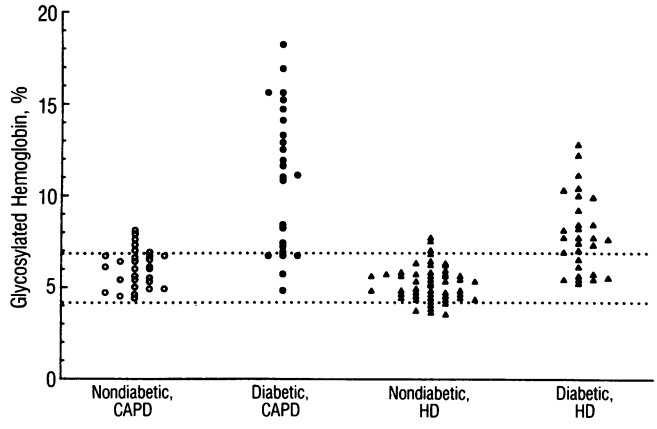

Figure 1.—The graph shows glycosylated hemoglobin levels in nondiabetic and diabetic patients on either continuous ambulatory peritoneal dialysis (CAPD) or hemodialysis (HD). Multiple (2 to 4) measurements for each patient are shown (n = 139). Interrupted lines show the upper and lower normal limits for the assay. For nondiabetic patients, CAPD measurements were statistically higher than hemodialysis measurements ($P < .005$, 2-tailed nonpaired t test).

that CAPD and hemodialysis therapy represent different states of both glucose metabolism—because patients on CAPD are never in a true fasting state—and azotemia and acidosis—because patients on hemodialysis therapy are not in a steady state for either of these two clinical conditions.

Results

Figure 1 shows glycosylated hemoglobin percentages in the four groups studied. Normal values for HbA_1 in this laboratory are between 4.0% and 6.8%. For nondiabetic patients on CAPD therapy, 95% confidence limits of HbA_1 were 5.5% and 6.8%. Few measurements were greater than 6.8%. All these measurements were from patients with impaired glucose tolerance. For nondiabetic patients receiving hemodialysis, 95% confidence limits for HbA_1 were 4.9% and 5.5%. Few measurements exceeded 6.8%, and all were obtained from patients with impaired glucose tolerance. Hemoglobin A_1 measurements were greater than 6.8% in 81% of the specimens from diabetic patients on CAPD therapy and in 68% of the specimens from diabetic patients receiving hemodialysis.

Table 1 shows the initial (beginning of the study) and final (after six months) blood hemoglobin concentrations. Blood hemoglobin levels remained stable in all four groups. Transfusions of packed red cells (two units each) were administered during the study period to one nondiabetic patient on CAPD therapy and two nondiabetic patients and one diabetic patient on hemodialysis therapy. In the four months before the study, no transfusions were administered. An external loss of blood or preparing for transplantation were the indications for transfusion in three of the four transfused patients.

TABLE 1.—*Initial and Final (After 6 Months) Blood Hemoglobin Concentration**

	Peritoneal Dialysis		Hemodialysis	
	Nondiabetic	Diabetic	Nondiabetic	Diabetic
Initial				
Range	66-119	80-130	56-125	54-104
Mean±SD ...	100±17	107±17	84±19	80±16
Final				
Range	62-126	83-135	62-135	57-110
Mean±SD ...	103±19	107±18	87±21	80±17
P†	NS	NS	NS	NS

NS=not significant, SD=standard deviation

*Grams per liter.
†Two-tailed, paired *t* test.

Table 2 shows fasting blood glucose levels, serum urea and creatinine concentrations, and total CO_2 content that were determined simultaneously with the glycosylated hemoglobin levels. For hemodialysis patients, serum urea, creatinine, and CO_2 concentrations are time-averaged. Statistical differences between the four groups are noted in the table. Table 3 shows the correlation matrix between HbA_1 levels and the other four variables. With the exception of the serum creatinine levels, all the "independent" variables correlated significantly with HbA_1 values. The fasting blood glucose level showed the highest correlation by far. Of note is the high degree of intercorrelation between the "independent" variables of blood glucose, creatinine, urea, and total CO_2 content. Figure 2 shows a linear regression between the fasting blood glucose and HbA_1 levels. To avoid superimposing many symbols, only the average of each patient is plotted. Linear regression with each pair of measurements providing one data point (n = 139) reveals essentially the same results. The correlation between daily average blood glucose and HbA_1 levels was .8732 (n = 26; $P < .01$). For the same 26 determinations of HbA_1, the correlation between the fasting blood glucose and HbA_1 levels was .7141 ($P < .01$)

Figure 2.—The graph shows the linear regression of fasting blood glucose levels on glycosylated hemoglobin levels. The average for each patient is plotted (n = 43) (Y = 2.29 + 0.64X; $r = .847$ [$P < .01$]). ○ = nondiabetic patients on continuous ambulatory peritoneal dialysis (CAPD) treatment, ● = diabetic patients on CAPD therapy, △ = nondiabetic patients on hemodialysis, ▲ = diabetic patients on hemodialysis

TABLE 2.—*Serum Concentrations Measured Concomitantly With Hemoglobin A_1 Determinations**

Patient Group/Therapy		Fasting Glucose, mmol/liter	Urea, mmol/liter	Creatinine, μmol/liter	Total Carbon Dioxide, mmol/liter
Nondiabetic/CAPD	Range	2.6-10.4	12.0-31.5	470-1,570	19.0-26.0
	Mean±SD	5.7±1.8	22.0±6.0	910±340	22.4±2.6
Diabetic/CAPD	Range	3.9-30.1	11.0-31.0	380-1,110	19.0-27.0
	Mean±SD	10.8±6.2	19.0±5.0	660±230	23.1±2.4
Nondiabetic/hemodialysis	Range	2.9-12.6	8.0-31.0	430-1,010	13.5-23.0
	Mean±SD	4.9±0.8	24.0±5.0	690±170	18.4±2.1
Diabetic/hemodialysis ...	Range	3.7-17.8	18.0-29.0	480-1,140	16.5-23.0
	Mean±SD	9.3±3.3	23.0±3.0	670±170	20.0±1.8
Normal values	Range	3.3-5.9	3.5-7.0	50-110	22.0-27.0

SD=standard deviation

*Statistically significant differences of the means (2-tailed, nonpaired *t* test) are as follows: **A**, within each dialysis modality (nondiabetic to diabetic): fasting blood glucose, continuous ambulatory peritoneal dialysis (CAPD) and hemodialysis, both at $P < .001$; urea, CAPD, $P < .05$; and creatinine, CAPD, $P < .005$. **B**, between dialysis modalities (CAPD to hemodialysis): total CO_2, all patients, $P < .001$; fasting blood glucose, only nondiabetic groups, $P < .01$.

TABLE 3.—*Correlating Matrix Between Glycosylated Hemoglobin Levels, Fasting Blood Glucose Levels, Serum Urea and Serum Creatinine Concentrations, and Serum Total Carbon Dioxide Content (n=139)*

		Blood Glucose	Serum Urea	Serum Creatinine	Total CO_2
Hemoglobin A_1,	r	.712	−.374	−.091	.315
	P	<.001	<.001	.285	.002
Blood glucose,	r		−.264	−.181	.242
	P		.002	.033	.004
Serum urea,	r			.402	−.516
	P			<.001	<.001
Serum creatinine,	r				−.046
	P				.589

and between the fasting blood glucose and average daily blood glucose levels was .7702 ($P<.01$).

The presence of the intercorrelations between the "independent" fasting variables made the use of the stepwise-regression procedure necessary. After logarithmic transformation of the data, four variables were shown to be related to the HbA_1 value in a statistically significant way. These were the fasting blood glucose and serum urea and creatinine levels and an interaction factor between the blood glucose and serum urea levels. Combined, these factors accounted statistically for .60 of the variability (R^2) in HbA_1 levels. The fasting blood glucose value alone accounted for .54 of this variability. A regression analysis was done three times including all the data after logarithmic transformation; excluding the outliers and with logarithmic transformation; and excluding the outliers, excluding the serum urea, and with logarithmic transformation. This analysis yielded essentially similar results. The R^2 remained around .60 in each analysis. The contribution of the fasting blood glucose level to this variability was around .50 in each analysis.

A comparison of the regression lines of the blood glucose on the HbA_1 value between CAPD and hemodialysis patients revealed that neither the regression coefficients nor the Y intercepts differed statistically between the dialysis populations.

Discussion

A tight control of blood glucose levels in diabetic patients on dialysis therapy may prevent a rapid acceleration of atherosclerosis[7] and a progression of microvascular complications.[15] Physicians and patients often do not estimate glycemic control accurately.[16,17] A reliable method of estimating HbA_1 levels in diabetic patients on dialysis therapy would have clinical use.

Chromatography is the most commonly used method of measuring HbA_1 levels. Carbamylated hemoglobin has similar negative electrical charges as some of the fractions of HbA_1 and cannot, therefore, be separated from HbA_1 by cation-exchange chromatography.[2,9,15,18-23] Affinity chromatography, which has been included among the chromatographic methods considered unsuitable for determining HbA_1 levels in uremic subjects,[3] does not measure carbamylated hemoglobin as part of the HbA_1. The affinity chromatographic column contains diimidazole-activated agar matrix to which aminophenylboronic acid is coupled. The HbA_1 is separated by a coupling of the boronate of the column with the glucose molecules that are attached to the globin moiety of HbA_1.[24,25] Several studies have shown agreement between HbA_1 measurements by boronate affinity chromatography and other indicators of glycemia in dialysis patients but raised the questions addressed by this study.[8,26,27]

The findings of this study are as follows:

- Hemoglobin A_1 levels are normal in nondiabetic persons on dialysis therapy.
- The statistically significant negative correlation between HbA_1 levels and the degree of azotemia and the positive correlation between HbA_1 levels and the total CO_2 content were due almost entirely to the statistical interactions between fasting blood glucose and serum urea levels and between the blood glucose levels and total CO_2 content.
- The indexes of glycemia correlated strongly with HbA_1 levels and accounted largely for their variability.

The normality of HbA_1 levels in nondiabetic persons on dialysis therapy can be the result of either normal blood glucose levels or a combination of uremic hemolysis, which decreases HbA_1 levels, and uremic glucose intolerance, which increases HbA_1 levels. Uremic glucose intolerance, however, is corrected to a great extent by adequate dialysis.[28] Furthermore, the finding that blood hemoglobin levels remained constant in this study with minimal amounts of transfusions militates against an accelerated rate of erythrocyte destruction. Although the question is not completely answered, our evidence suggests that the normal HbA_1 levels in nondiabetic patients receiving dialysis do not result from a combination of uremic hemolysis and uremic glucose intolerance.

The correlations between fasting blood glucose levels and the variables indicating azotemia and acidosis reflect the fact that for diabetic patients, dialysis therapy is started earlier than for nondiabetic patients,[29] and they have, consequently, lower serum urea and higher serum CO_2 levels (Table 2). The small but independent effect of the serum creatinine value on the statistical variability of HbA_1 levels found in the stepwise-regression procedure reflects in part the earlier initiation of dialysis therapy in diabetic patients and the debilitated state often present in diabetic patients on dialysis therapy.[30]

Finally, the process of glycosylation appears to be similar between CAPD and hemodialysis, despite dissimilarities in availabilities of glucose (continuous versus intermittent), in acid-base control, and in the control of azotemia. As expected, both fasting blood glucose and HbA_1 levels were higher in patients receiving CAPD than in those receiving hemodialysis. Yet the regression of blood glucose levels on HbA_1 levels did not differ between the two treatments. These findings are consistent with the hypothesis that glycemia is the only important variable in HbA_1 formation in dialysis patients. In vitro findings are also consistent with this hypothesis.[10]

We suggest that HbA_1 levels should be measured by affinity chromatography in persons on dialysis therapy when there is doubt about glucose control and routinely in diabetic patients at infrequent intervals—for example, every six months. This method also provides an objective means of assessing glycemic control when specific interventions are studied, as when the intraperitoneal administration of insulin is compared with subcutaneous insulin for blood glucose control of diabetic patients on CAPD therapy.

REFERENCES

1. Bunn HF, Gabbay KH, Gallop PM: The glycosylation of hemoglobin: Relevance to diabetes mellitus. Science 1978; 200:21-27

2. Fluckiger R, Harmon W, Meier W, et al: Hemoglobin carbamylation in uremia. N Engl J Med 1981; 304:823-827

3. Health and Public Policy Committee, American College of Physicians: Glycosylated hemoglobin assays in the management and diagnosis of diabetes mellitus. Ann Intern Med 1984; 101:710-713

4. Tzamaloukas AH: Diabetes, chap 24, *In* Daugirdas JT, Ing TS (Eds): Handbook of Dialysis. Boston, Little, Brown, 1988, pp 321-330

5. De Fronzo RA, Smith D, Alvestrand A: Insulin action in uremia. Kidney Int 1983; 24 (suppl 16):S102-S114

6. Panzer S, Kronik G, Lechner K, et al: Glycosylated hemoglobins (GHb): An index of red cell survival. Blood 1982; 59:1348-1350

7. De Fronzo RA, Smith JD: Is glucose intolerance harmful for the uremic patient? Kidney Int 1985; 28 (suppl 17):S88-S97

8. Bruns DE, Lobo PI, Savory J, et al: Specific affinity-chromatographic measurement of glycated hemoglobins in uremic patients. Clin Chem 1984; 30:569-571

9. De Marchi S, Cecchin E, Basile A, et al: More on the increase of hemoglobin A_1 in chronic renal failure: The role of acidosis. Nephron 1983; 35:49-53

10. Wettre S, Lundberg M: Kinetics of glycosylated haemoglobin in uraemia determined on ion-exchange and affinity chromatography: No increase in the rate of glycosylation. Diabetes Res 1986; 3:107-110

11. National Diabetes Data Group: Classification and diagnosis of diabetes mellitus and other categories of glucose intolerance. Diabetes 1979; 28:1039-1057

12. Sargent JA, Gotch FA: The analysis of concentration dependence of uremic lesions in clinical studies. Kidney Int 1975; 7 (suppl 2):S35-S44

13. Tietz N: Textbook of Clinical Chemistry. Philadelphia, WB Saunders, 1986

14. Stepwise Procedure, Statistical Analysis System Users' Guide. Raleigh, NC, SAS Institute, 1979, pp 391-396

15. Amair P, Khanna R, Leibel B, et al: Continuous ambulatory peritoneal dialysis in diabetics with end-stage renal disease. N Engl J Med 1982; 306:625-630

16. Nathan DM, Singer DE, Hurxthal K, et al: The clinical information value of the glycosylated hemoglobin assays. N Engl J Med 1984; 310:341-346

17. Mazze RS, Shannon H, Pasmantier R, et al: Reliability of blood glucose monitoring by patients with diabetes mellitus. Am J Med 1984; 77:211-217

18. De Boer MJ, Miedema K, Kasparie AF: Glycosylated hemoglobin in renal failure. Diabetologia 1980; 18:437-440

19. Oimomi M, Yoshimura Y, Kabota S, et al: Hemoglobin A_1 properties of diabetic and uremic patients. Diabetes Care 1981; 4:484-486

20. Hirszel P, Galen MA, Harpe T, et al: Glycosylated hemoglobin in patients treated by chronic dialysis. Int J Urol Nephrol 1981; 13:185-191

21. Panzetta G, Bassetto MA, Feller P, et al: Micro-chromatographic measurement of hemoglobin A_1 in uremia. Clin Nephrol 1983; 20:259-262

22. Oimomi M, Ishikawa K, Kawasaki T, et al: Carbamylation of hemoglobin in renal failure and clinical aspects. Metabolism 1984; 33:999-1002

23. Saloranta C, Groop L, Ylinen K, et al: The usefulness of micro- and macrochromatographic determinations of glycohemoglobin in diabetic patients with nephropathy. Clin Nephrol 1986; 25:186-192

24. Mallia AK, Hermanson GT, Krohn RI, et al: Preparation and use of a boronic acid affinity support for preparation and quantitation of glycosylated hemoglobin. Anal Lett 1981; 14:649-661

25. Yue DK, McLennon S, Church DM, et al: The measurement of glycosylated hemoglobin in man and animals by aminophenylboronic acid affinity chromatography. Diabetes 1982; 21:701-705

26. Bannon P, Lessard F, Lepage R, et al: Glycated hemoglobin in uremic patients as measured by affinity and ion-exchange chromatography. Clin Chem 1984; 30:485-486

27. Scott MG, Hoffmann JW, Meltzler VN, et al: Effects of azotemia on results of the boronate-agarose affinity and ion-exchange methods for glycated hemoglobin. Clin Chem 1984; 30:896-898

28. Castellino P, De Fronzo RA, Giordano C: Glucose metabolism and insulin metabolism in CAPD patients (Abstr). Peritoneal Dial Bull 1987; 7:S13

29. Massry SG, Feinstein EI, Goldstein DA: Early dialysis in diabetic patients with chronic renal failure. Nephron 1979; 23:2-5

30. Avram MM: Lower parathyroid hormone and creatinine in diabetic uremia. Contrib Nephrol 1980; 20:4-8

Diuretic-Induced Gout

WE ARE SEEING SOMETHING NEW IN GOUT that is very interesting—it is called diuretic-induced gout. We are finding this in a population over the age of 70, as opposed to the usual gout sufferer, who is usually about 40. We are seeing women more commonly than men, which is a total reverse.

These patients have acute attacks, frequently in the hands and knees. Basically, these are elderly women on diuretics with Heberden's or Bouchard's nodes, coming in with some tophaceous deposits in these little osteoarthritic changes in the hands, and this is so-called diuretic-induced gout. Many times these patients have mild renal insufficiency, and it is something you want to think about. They come in with this acute inflammatory process in their hands. If they have osteoarthritis, but it looks too inflammatory for mere osteoarthritis or even an erosive osteoarthritis, think about diuretic-induced gout.

—STEVEN R. WEINER, MD

Extracted from *Audio-Digest Emergency Medicine*, Vol. 5, No. 21, in the Audio-Digest Foundation's series of tape-recorded programs. For subscription information: 1577 E Chevy Chase Dr, Glendale, CA 91206